

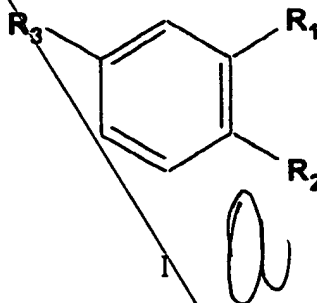
WHAT IS CLAIMED IS:

1. A nitrosated and/or nitrosylated phosphodiesterase inhibitor having the formula $\text{NO}_n\text{-PDE}$ wherein is 1 or 2.

2. The nitrosated and/or nitrosylated phosphodiesterase inhibitor of claim 1 which is nitrosylated or nitrosated through an oxygen, sulfur, carbon or nitrogen site on the phosphodiesterase inhibitor.

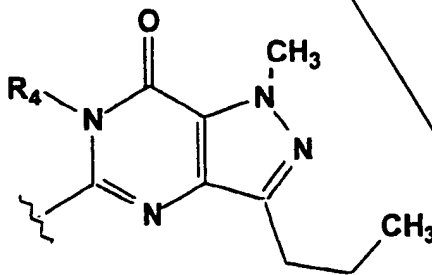
3. The nitrosated and/or nitrosylated phosphodiesterase inhibitor of claim 1 which is selected from the group consisting of:

(I) compounds having the structure:



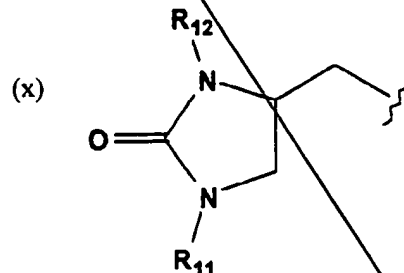
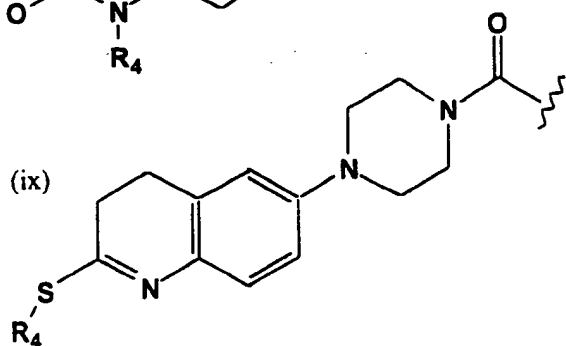
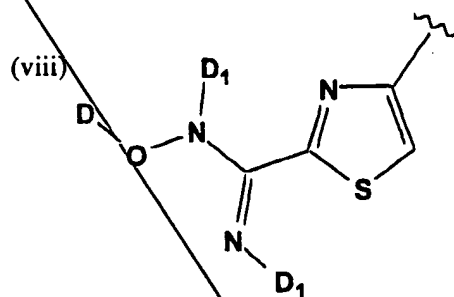
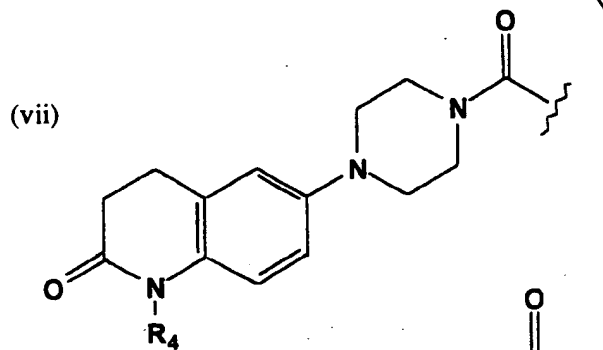
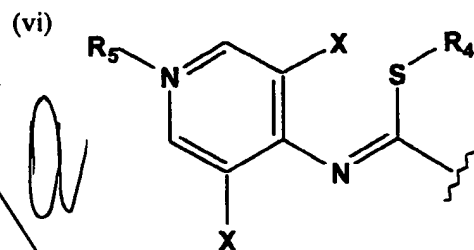
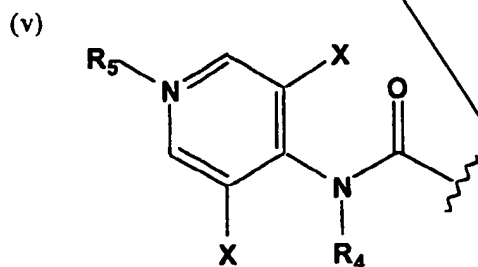
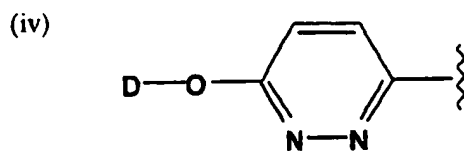
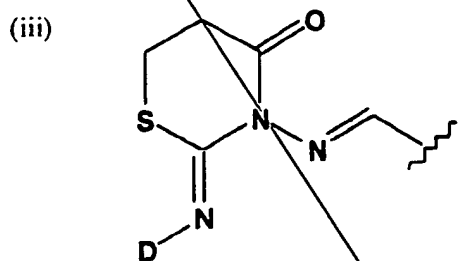
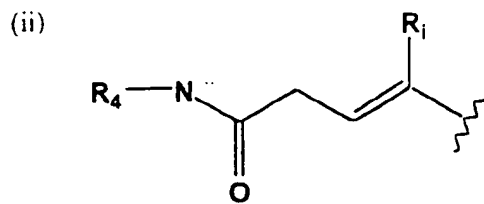
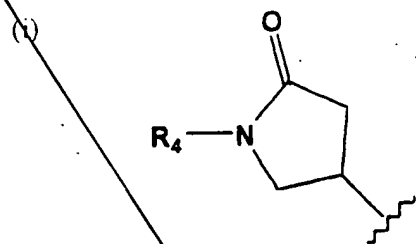
wherein,

R_1 is alkoxy, cycloalkoxy, halogen, or



R_2 is hydrogen, alkoxy, or haloalkoxy; and

R_3 is selected from:



wherein

D is selected from (i) -NO; (ii) -NO₂; (iii) -C(R_d)-O-C(O)-Y-Z-[C(R_e)(R_f)]_p-T-Q in which R_d is hydrogen, lower alkyl, cycloalkyl, aryl, alkylaryl, aryl or heteroaryl, Y is oxygen, sulfur, or NR_i in which R_i is hydrogen, lower alkyl, R_e and R_f at each occurrence are independently selected from hydrogen, lower alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, amino, alkylamino, amido, alkylamido, dialkylamino, carboxy, or taken together are carbonyl, cycloalkyl or bridged cycloalkyl, p is an integer from 1 to 6, T is a covalent bond, oxygen, sulfur or nitrogen, Z is selected from a covalent bond, alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl or arylheterocyclic ring, and Q is selected from -NO or -NO₂; (iv) -C(O)-T¹-Z-[C(R_e)(R_f)]_p-T²-Q wherein T¹ and T² are independently selected from T and R_e, R_f, p, Q, Z, and T are as defined in this specification; (v) -C(O)-Z-[G-[C(R_e)(R_f)]_p-T-Q]_p wherein G is (i) a covalent bond; (ii) -T-C(O)-; (iii) -C(O)-T, or (iv) Y, and wherein R_e, R_f, p, Q, T, Y, and Z are as defined in this specification; (v) -C(O)-T[C(R_y)(R_z)]_p wherein R_y and R_z are independently selected from -T¹-[C(R_e)(R_f)]_p-G-[C(R_e)(R_f)]_p-T²-Q wherein G, R_e, R_f, p, Q, T, T¹, and T² are as defined in this specification;

R₄ is selected from (i) hydrogen, (ii) -C(R_d)-O-C(O)-Y-Z-[C(R_e)(R_f)]_p-T-Q, (iii) -C(O)-T¹-[C(R_e)(R_f)]_p-T²-Q, (iv) -C(O)-Z-[G-[C(R_e)(R_f)]_p-T-Q]_p; and wherein R_d, R_e, R_f, p, G, T, T¹, T², Q, Y, and Z are defined as in this specification;

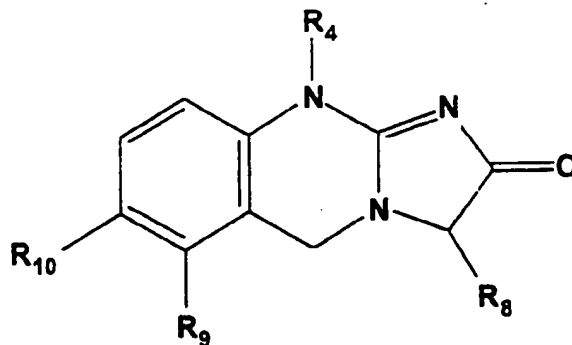
R₅ is selected from a lone pair of electrons or -C(R_d)-O-C(O)-Y-Z-[C(R_e)(R_f)]_p-T-Q wherein R_d, R_e, R_f, p, T, T¹, T², Q, Y, and Z are defined as in this specification;

R₁₁ and R₁₂ are independently selected from hydrogen or R₄ wherein R₄ is as defined in this specification with the provision that R₁₁ and R₁₂ are not both hydrogen;

X is a halogen and;

D₁ is selected from D or hydrogen and wherein D is as defined in this specification.

(1) compounds having the structure:



II

wherein,

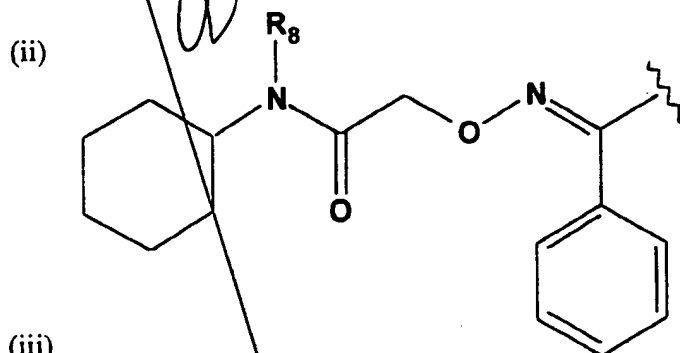
R_4 is as defined in this specification;

R_8 is selected from hydrogen or lower alkyl;

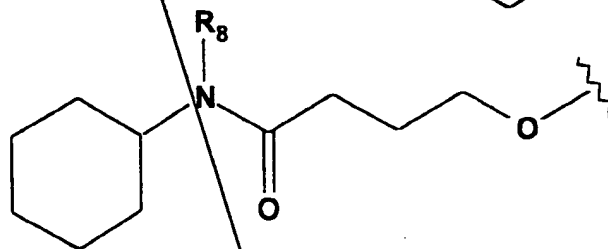
R₉ is selected from hydrogen or halogen; and

R_{10} is selected from:

(i) hydrogen

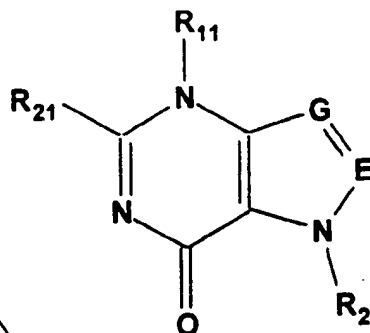


(iii)



wherein R_8 is as defined in this specification.

(III) compounds having the structure:



III

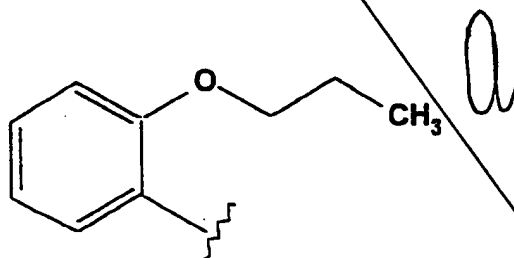
wherein,

E is selected from nitrogen or -CH-;

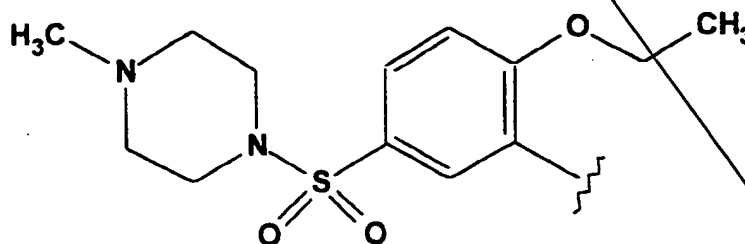
G is selected from nitrogen or -C(R₈)-;

R₂₁ is selected from:

(i)



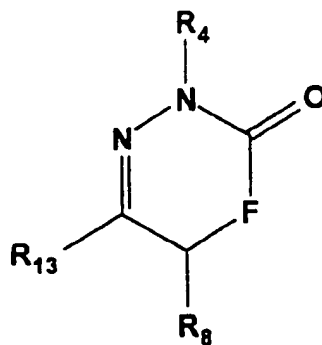
(ii)



R₂₂ is selected from R₁₂ or lower alkyl; and

R₈, R₁₁, and R₁₂ are as defined in this specification.

(IV) compounds having the structure:



IV

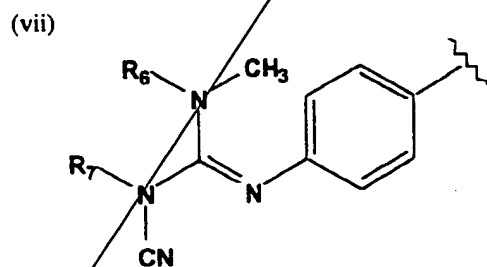
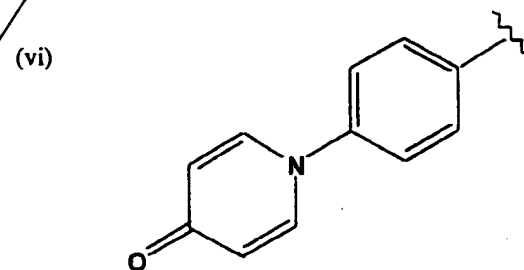
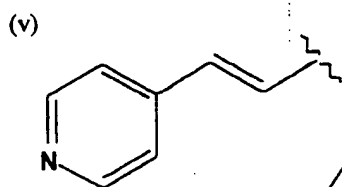
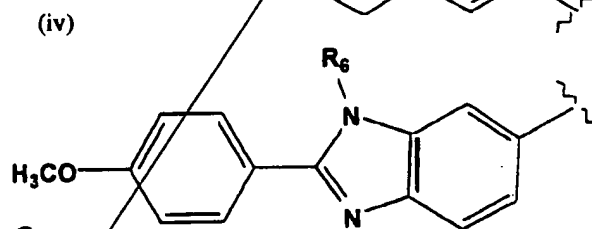
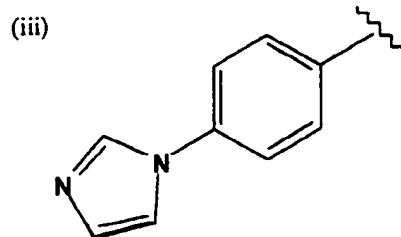
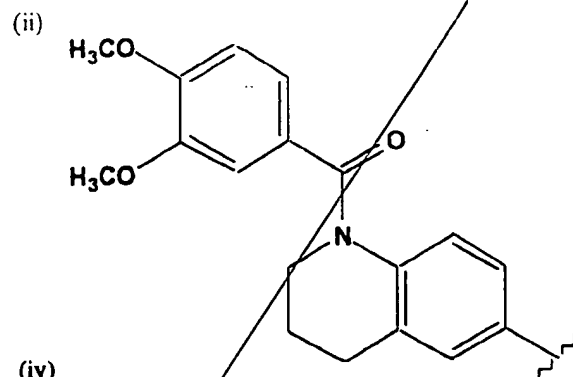
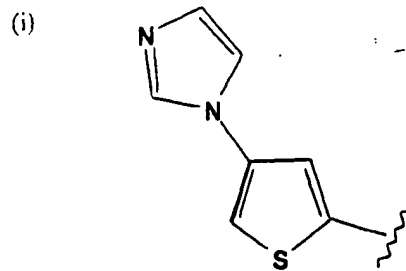
wherein,

F is selected from -CH₂- or sulfur;

R₄ and R₈ are as defined in this specification; and

R₁₃ is selected from:

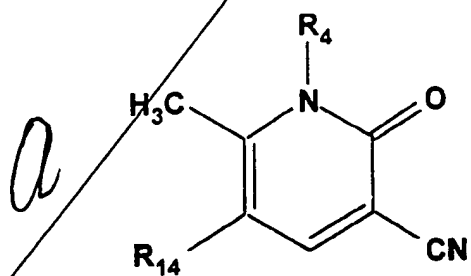
a



wherein,

R_6 and R_7 are independently selected from hydrogen or R_4 wherein R_4 is as defined in this specification.

(V) compounds having the structure:



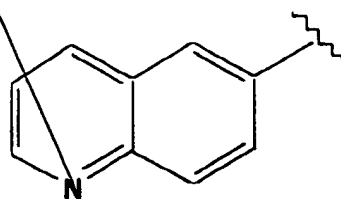
V

wherein,

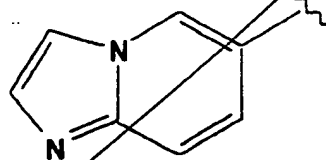
R_4 is as defined in this specification; and

R_{14} is selected from:

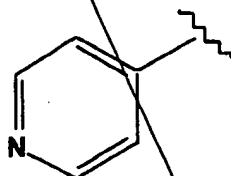
(i)



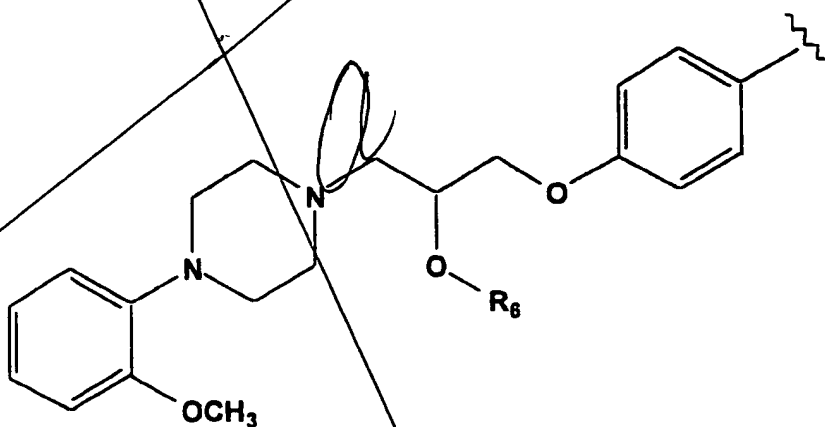
(ii)



(iii)

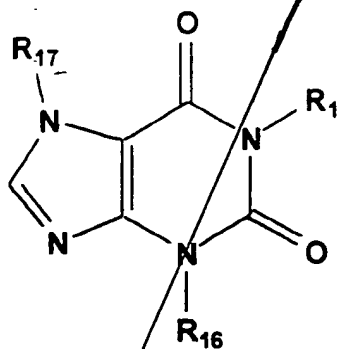


(iv)



wherein R_6 is as defined in this specification.

(VI) compounds having the structure:



VI

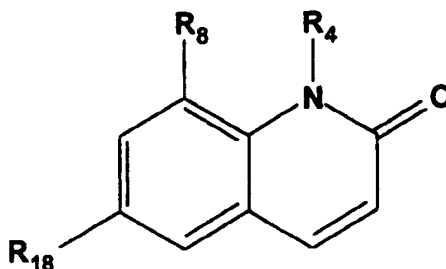
wherein,

R_{15} is hydrogen, lower alkyl, R_4 , or $-(CH_2)_4-C(CH_3)_2-O-D_1$;

R_{16} is lower alkyl; and

R_{17} is hydrogen, lower alkyl, $CH_3-C(O)-CH_2-$, CH_3-O-CH_2- , or D with the provision that either R_{15} or R_{17} must be selected to contain D and wherein D and D_1 are as defined in this specification.

(VII) compounds having the structure:



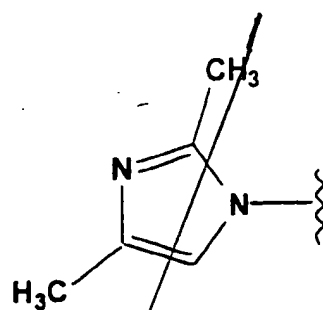
VII

wherein,

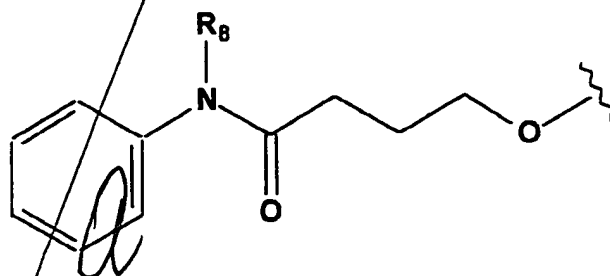
R_4 and R_8 are as defined in this specification and

R_{18} is selected from:

(i)

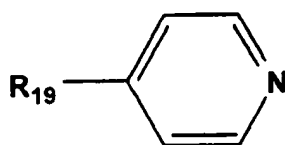


(ii)



and wherein R₈ is as defined in this specification.

(VIII) compounds having the structure:

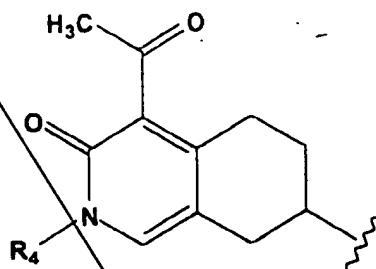


VIII

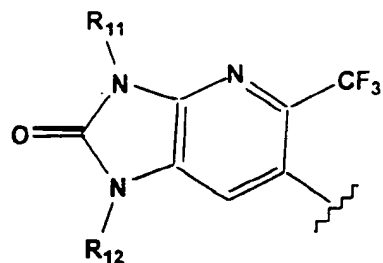
wherein,

R₁₉ is selected from:

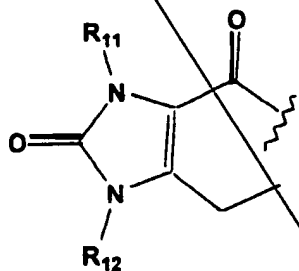
(i)



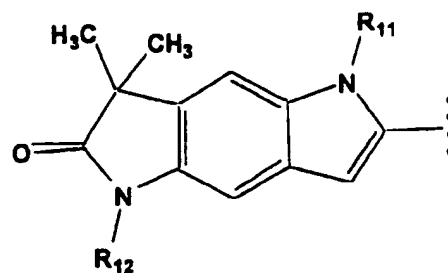
(ii)



(iii)

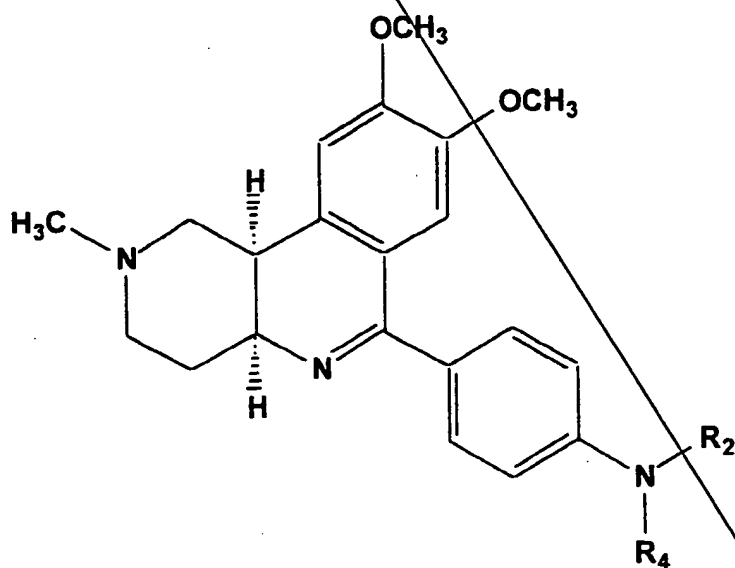


(iv)



and wherein R_4 , R_{11} , and R_{12} are defined as in this specification.

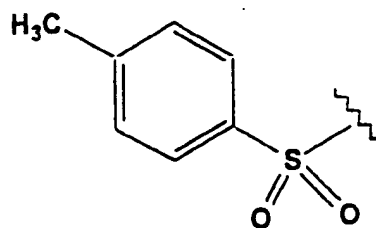
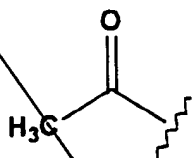
(IX) compounds having the structure:



IX

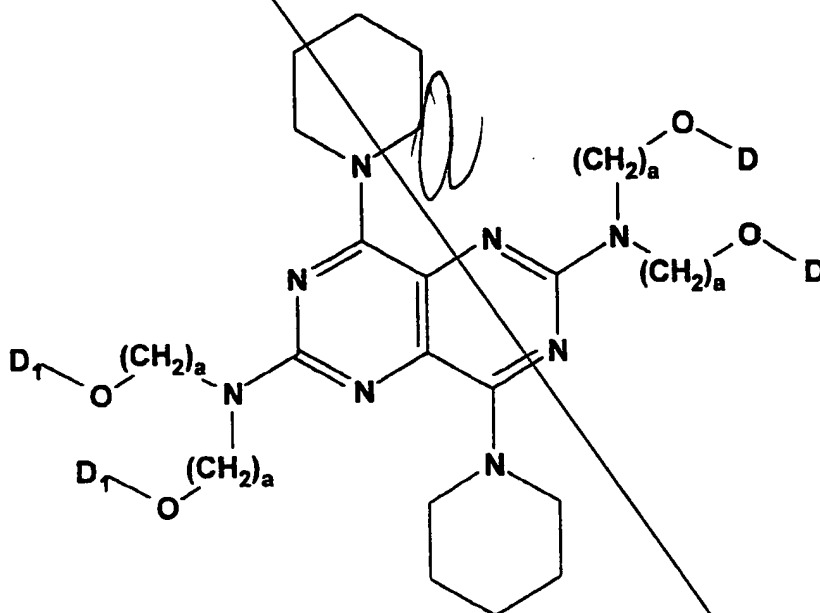
~~wherein.~~

R_{20} is selected from:



and wherein R_4 is defined as in this specification.

(X) compounds having the structure:

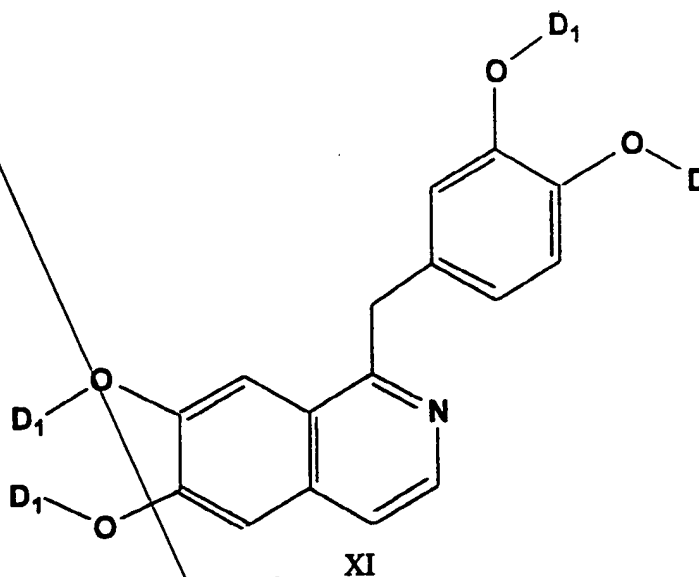


x

wherein,

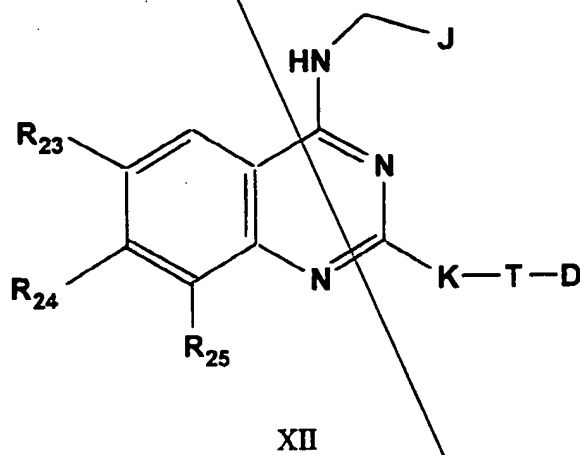
a is an integer from 2 to 3 and D and D_1 are defined as in this specification.

(XI) compounds having the structure:



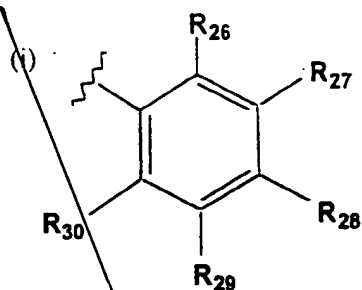
wherein D and D₁ are defined as in this specification.

(XII) compounds having the structure:

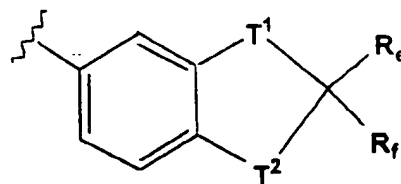


wherein,

J is selected from:

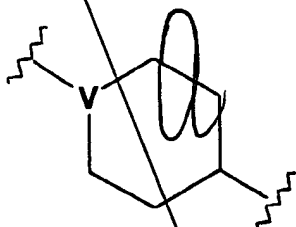


(ii)

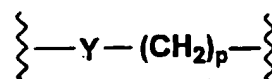


K is selected from:

(i)



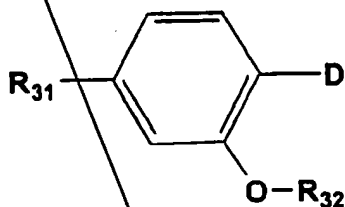
(ii)



wherein V is carbon or nitrogen;

R_{23} , R_{24} , R_{25} , R_{26} , R_{27} , R_{28} , R_{29} , and R_{30} are independently selected from hydrogen, halogen, alkoxy, nitrile, carboxamido, or carboxyl; and wherein p , R_e , R_f , T , T^1 , T^2 , Y and D are defined as in this specification.

(XIII) compounds having the structure:



XIII

wherein,

 R_{31} is alkyl, halogen, haloalkyl, or haloalkoxy; R_{32} is selected from D_1 or $-C(O)-R_8$; and

wherein D_1 and R_8 are defined as in this specification.

4. A composition comprising a therapeutically effective amount of the phosphodiesterase inhibitor of claim 1 and a one to ten fold molar excess of a compound that donates, transfers or releases nitrogen monoxide as a charged species, i.e., nitrosonium (NO^+), or nitroxyl (NO^-), or as the neutral species, nitric oxide (NO^\bullet) or induces the production of endogenous EDRF and a pharmaceutically acceptable carrier.

5. A method for treating male impotence in humans which comprises administering to an individual in need thereof a therapeutically effective amount of a nitrosated or nitrosylated PDE inhibitor of claim 1.

6. A method for treating female sexual dysfunction in humans which comprises administering to an individual in need thereof a therapeutically effective amount of a nitrosated or nitrosylated PDE inhibitor of claim 1.

7. A method for treating anal disease in humans which comprises administering to an individual in need thereof a therapeutically effective amount of a nitrosated or nitrosylated PDE inhibitor of claim 1.

Appendix 1 – Pending Claims

a¹ 8. (New) A method of treatment, in an organism, of a vascular condition, comprising administration of at least one agent at a level which enhances NO and which does not appreciably alter normal systemic vascular tone in said organism.

9. (New) A method for treating sexual dysfunction in a female individual, comprising administering to the vagina, vulvar area and/or urethra of the individual a pharmaceutical formulation that comprises an effective amount of a nitrovasodilator selected from the group consisting of sodium nitroprusside, diazenium diolates, molsidomine, linsidomine chlorohydrate, S-nitrosothiols, organic nitrates, pharmacologically acceptable salts, esters, analogs, derivatives, prodrugs and inclusion complexes of any of the foregoing, and combinations thereof.

10. (New) A method of enhancing sexuality in a female having a clitoris comprising the step of topically administering to a surface of the clitoris a composition whose primary agent is a vasodilator and whose secondary agent is a carrier in which the vasodilator is dispersed to deliver it directly to said surface so that it is retained and absorbed thereby, said composition being in a formulation and in a dosage which is substantially free of toxicity and therefore does not give rise to an adverse reaction.